

## **Listing of the Claims**

1. (original): A method for delivery of substance through at least one dermal layer, the method comprising:

providing a substance in microcapsules at a predetermined size, within a medium for holding the microcapsules;

placing the medium for holding the microcapsules on a surface of a patch adjacent the skin of a human or animal; and

applying energy to the patch, the energy having a characteristic of disturbing the integrity of the microcapsules, thereby resulting in release of the substance from the microcapsules.

2. (original): The method of claim 1, wherein the energy applied to the patch includes thermal energy.

3. (original): The method of claim 1, wherein the energy applied to the patch includes ultrasonic energy applied to the patch at a resonant frequency for certain or all of the microcapsules, thereby rupturing them.

4. (original): The method of claim 3, wherein the patch includes a top surface which is relatively impermeable to the medium, wherein the medium is surrounded along an outer perimeter with an adhesive matrix, thereby substantially containing the microcapsules within the medium and further substantially containing the substance to be delivered within the patch prior to activation by application of said ultrasonic energy.

5. (original): The method of claim 3, wherein the microcapsules have diameters of approximately 0.003 mm and a resonance frequency of approximately 2000 kHz.

6. (original): The method of claim 3, wherein a rate of release of the substance is

controlled in a precise manner by the localized application of the energy.

7. (original): The method of claim 3, wherein certain of the microcapsules have a first resonant frequency and other of the microcapsules have a second resonant frequency, and the release of substance from the microcapsules is controlled by selective application of ultrasonic energy at the first and at the second resonance frequency.

8. (original): The method of claim 3, wherein:

the substance for delivery is a pharmaceutical substance provided for transdermal drug delivery; and

the substance is activated by a patient controlling the application of the energy.

9. (original): The method of claim 3, wherein said substance includes at least one of: drug, biologically active compound, excipient, skin permeation enhancer.

10. (original): The method of claim 3, wherein said substance includes insulin provided for transdermal delivery.

11. (original): The method of claim 3, wherein said substance includes a vitamin.

12. (original): The method of claim 3, wherein said substance includes skin permeation enhancer.

13. (original): The method of claim 3, wherein the medium for holding the microcapsules includes skin permeation enhancer.

14. (previously presented): The method of claim 3, wherein the energy applied to the patch includes thermal energy.

15 – 51 (canceled)

52. (currently amended): A method of delivering an agent encapsulated in microspheres or nanospheres in a patch matrix comprising the use of ultrasound at a resonant frequency between 0.1 and 100 MHz to rupture the ~~micro-microspheres~~ or nanospheres, thereby releasing the agent into the patch matrix.

53. (previously presented): The method of claim 52 wherein the agent comprises at least one of: drug, biologically active compound, excipient, skin permeation enhancer.

54. (currently amended): A method of delivering an agent encapsulated in microspheres or nanospheres in a patch matrix comprising the use of heat to melt the ~~spheres-microspheres or nanospheres~~, to thereby release the agent.

55 – 56. (canceled)

57. (previously presented): The method of the controlled transdermal delivery of an agent encapsulated in microcapsules in a transdermal patch as a result of a controlled activation of the of the microcapsules in the transdermal patch using an ultrasound source or a heat source.

58. (previously presented): The method of claim 57, wherein the agent comprises insulin.

59. (previously presented): The method of claim 57, wherein the agent comprises vitamin.

60. (previously presented): The method of claim 57, wherein the agent comprises

skin permeation enhancer.

61. (previously presented): The method of claim 57, wherein the agent comprises any one or combination of the following:

anti-fungal agent, hormone, vitamin, peptide, enzyme, anti-allergic agent, anti-coagulation agent, antitubercular, antiviral, antibiotic, antibacterial, anti-inflammatory agent, antiprotozoan, local anesthetic, growth factor, cardiovascular agent, diuretic, radioactive compound, scopolamine, nicotine, methylnicotinate, mechlorisone dibutyrate, naloxone, methanol, caffeine, salicylic acid, and 4-cyanophenol.

62. (previously presented): The method of claim 61, wherein the anti-fungal agent is ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, or amphotericin B; and wherein the hormone is growth hormone, melanocyte stimulating hormone, estradiol, progesterone, testosterone, cyclomethasone dipropionate, betamethasone, betamethasone acetate, betamethasone sodium phosphate, betamethasone disodium phosphate, betamethasone sodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunisolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetate, triamcinolone diacetate, triamcinolone hexacetonide, or fludrocortisone acetate; and wherein the vitamin is cyanocobalamin, ascorbic acid, retinoid, retinol, palmitate, ascorbic acid,  $\alpha$ -tocopherol, or vitamin B-12; and wherein the enzyme is manganese superoxide dismutase or alkaline phosphatase; and wherein the anti-allergic agent is amlexanox; and wherein the anti-coagulation agent is phenprocoumon or heparin; and wherein the antitubercular is paraminosalicic acid, isoniazid, capreomycin sulfate, cycloserine, ethambutol hydrochloride

ethionamide, pyrazinamide, rifampicin, or streptomycin sulfate; and wherein the antiviral is acyclovir, amantadine azidothymidine, ribavirin or vidarabine monohydrate; and wherein the antibiotic is dapsone, chloramphenicol, neomycin, cefaclor, cefadroxil, cephalexin, cephadrine, erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxacillin, cyclacillin, picloxacillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin G, penicillin V, ticarcillin, rifampin or tetracycline; and wherein the anti-inflammatory is diflunisal, ibuprofen, indomethacin, meclofenamate, mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam, diclofenac, sulindac, tolmetin, aspirin or salicylate; and wherein the antiprotozoan is chloroquine, hydroxychloroquine, metronidazole, quinine or meglumine antimonate; and wherein the local anesthetic is bupivacaine hydrochloride, chloroprocaine hydrochloride, etidocaine hydrochloride, lidocaine hydrochloride, mepivacaine hydrochloride, procaine hydrochloride or tetracaine hydrochloride; and wherein the growth factor is Epidermal Growth Factor, Acidic Fibroblast Growth Factor, Basic Fibroblast Growth Factor, Insulin-Like Growth Factor, Nerve Growth Factor, Platelet-Derived Growth Factor, Stem Cell Factor, Transforming Growth Factor of the  $\alpha$  family or Transforming Growth Factor of the  $\beta$  family; and wherein the cardiovascular agent is clonidine, propranolol, lidocaine, nicardipine or nitroglycerin; and wherein the diuretic is mannitol or urea; and wherein the radioactive compound is a compound of radioactive strontium, iodine, rhenium or yttrium.